Quorum Sensing in *Burkholderia Cenocecapia*

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**Abstract**

Quorum sensing (QS) is widely employed by bacterial pathogens to coordinate bacterial group behavior and regulate biological functions such as biofilm formation, motility, virulence, plasmid transfer, and antibiotic production. Several types of QS systems have been identified including the most-characterized acylhomoserine lactone (AHL) dependent QS system and the relatively newly identified diffusible signal factor (DSF) dependent QS system. The AHL- and DSF-QS systems are mainly conserved in different Gram-negative bacteria pathogens. While most bacterial pathogens employ either AHL- or DSF-dependent QS systems in regulation of virulence and biofilm formation, we found that in addition to AHL signals, *Burkholderia cepacia* complex also produces DSF-type QS signals. In *B. cenocecapia*, which is an opportunistic pathogen in cystic fibrosis and immunocompromised patients, we showed that the QS signal synthase, RpfF, catalyzes the production of BDSF signal (cis-2-dodecenoic acid), which is an analogue of the QS signal DSF (cis-11-methyl-2-dodecenoic acid), originally identified in the plant bacterial pathogen *Xanthomonas campestris* pv. *campestris*. Our recent study showed that BDSF acts by interacting with its receptor RpfR, which is a modular protein with PAS-GGDEF-EAL domains. Perception of BDSF by RpfR sharply enhances its c-di-GMP phosphodiesterases activity and consequently causes a reduction in the intracellular level of the second messenger cyclic dimeric guanosine monophosphate (c-di-GMP) in *B. cenocecapia*, which consequently affects a range of biological activities, including swarming motility, biofilm formation and virulence. Our work presents a novel and widely conserved DSF-family signal receptor which directly links the signal perception to c-di-GMP turnover in regulation of bacterial physiology. In addition, we have also determined the molecular mechanisms with which the AHL and BDSF signaling system act to influence the bacterial virulence.

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